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EXAMINER	
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ART UNIT	PAPER NUMBER
1647	

MAIL DATE	DELIVERY MODE
11/25/2008	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/525,743	ELLIOTT, VICKI S.	
	Examiner	Art Unit	
	JON M. LOCKARD	1647	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *15 September 2008*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *126-143* is/are pending in the application.

4a) Of the above claim(s) *133-143* is/are withdrawn from consideration.

5)☒ Claim(s) *126 and 127* is/are allowed.

6)☒ Claim(s) *128-130 and 132* is/are rejected.

7)☒ Claim(s) *131* is/are objected to.

8)☒ Claim(s) *126-143* are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Election/Restrictions

1. This application contains claims drawn to an invention nonelected with traverse in the reply filed on 21 February 2008. A complete reply to the final rejection must include cancellation of nonelected claims or other appropriate action (37 CFR 1.144) See MPEP § 821.01.

Status of Application, Amendments, and/or Claims

2. The Amendment filed 15 September 2008 has been entered in full. Claims 126-130 and 132 have been amended. Therefore, claims 126-143 are pending, and claims 126-132 are the subject of this Office action.

3. The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

Withdrawn Objections and/or Rejections

4. The rejection of claims 126-132 under 35 U.S.C. § 112, 1st Paragraph (Scope of Enablement and Written Description) as set forth at pg 3-10 of the previous Office action (mailed 14 May 2008) is withdrawn in view of Applicant's amendment of claims 126-130 and 132 (filed 15 September 2008).

5. The rejection of claims 126-127 and 129-131 under 35 U.S.C. § 102(b) as set forth at pg 11-12 of the previous Office action (mailed 14 May 2008) are withdrawn in view of amended claims 126, 127, 129, and 130 (filed 15 September 2008).

New Objections and/or Rejections

Claim Objections

6. Claim 131 is objected to because of the following informalities: Although not indefinite, it is suggested for the purpose of clarity that claim 131 be amended to recite, for example, "The isolated polypeptide of claim 126…". Appropriate correction is suggested.

Claim Rejections - 35 USC § 112, 1st Paragraph (New Matter)

7. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

8. Claims 128-131 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. **This is a new matter rejection**.

9. Claim 128 recites the limitation "wherein the fragment is selected from the group consisting of: M1-P27, M1-V21, M1-A25, M1-F26, I57-R161, L16-P27, E87-Q131, Q131-R161, S80-R147, Q56-T71, C72-M95, C101-L126, I145-R161, Q56-C72, C78-G100, C101-T122, L144-R161, I57-I115, M1-K55, M1-T117, E108-M163, N107-M163, K110-R161, A28-M163, L22-M163, F26-M163, P27-M163 and combinations thereof". Claim 129 recites the

limitation "wherein one or more amino acid differences between SEQ ID NO: 1 and the variant are selected from the group consisting of amino acid positions 1-27, 50, 80, 148, 156, 71,116, 73 and 123 of SEQ ID NO: 1". Claim 130 recites the limitation "uniquely identifies". After extensive review, the Examiner is unable to find, in the Specification as originally filed, support for these newly added limitations. These newly added limitations are not expressly asserted, nor do they flow naturally from the Specification as originally filed. With regard to claims 128 and 129, Table 3 of the Specification as asserted by Applicant at pg 6 of the response (filed 15 September 2008) is noted. However, while it appears from the brief description of Table 3 at paragraph [0113] that Table 3 characterizes the full-length polypeptide of SEQ ID NO:1, such does not provide support for specific fragments or variants of SEQ ID NO:1. Furthermore, the specification at paragraph [0148] only provides support for fragments of SEQ ID NO:2 that specifically identifies SEQ ID NO:2, not for fragments of SEQ ID NO:2 that uniquely identifies SEQ ID NO:2.

Claim Rejections - 35 USC § 112, 1st Paragraph (Scope of Enablement)

10. Claims 128-130 and 132 are rejected under 35 U.S.C. § 112, first paragraph, because the specification, while being enabling for (1) an isolated polypeptide consisting or comprising *the* amino acid sequence SEQ ID NO:1, or (2) an isolated polypeptide encoded by a polynucleotide consisting or comprising *the* nucleic acid sequence SEQ ID NO:2, does not reasonably provide enablement for an isolated polypeptide (1) comprising a fragment of SEQ ID NO:1, wherein the fragment is selected from the group consisting of: M1-P27, M1-V21, M1-A25, M1-F26, I57-R161, L16-P27, E87-Q131, Q131-R161, S80-R147, Q56-T71, C72-M95, C101-L126, I145-

R161, Q56-C72, C78-G100, C101-T122, L144-R161, I57-I115, M1-K55, M1-T117, E108-M163, N107-M163, K110-R161, A28-M163, L22-M163, F26-M163, P27-M163 and combinations thereof; (2) an isolated polypeptide variant of SEQ ID NO:1, wherein one or more amino acid differences between SEQ ID NO: 1 and the variant are selected from the group consisting of amino acid positions 1-27, 50, 80, 148, 156, 71,116, 73 and 123 of SEQ ID NO: 1; or (3) an isolated polypeptide encoded by a polynucleotide comprising a portion of the polynucleotide sequence of SEQ ID NO:2 that uniquely identifies SEQ ID NO:2. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention commensurate in scope with these claims.

11. The specification's disclosure is insufficient to enable one skilled in the art to practice the invention as broadly claimed without undue experimentation. The factors considered when determining if the disclosure satisfies the enablement requirement and whether any necessary experimentation is "undue" include, but are not limited to: 1) nature of the invention, 2) state of the prior art, 3) relative skill of those in the art, 4) level of predictability in the art, 5) existence of working examples, 6) breadth of claims, 7) amount of direction or guidance by the inventor, and 8) quantity of experimentation needed to make or use the invention. In re Wands, 858 F.2d 731, 737, 8 USPQ2d 1400, 1404 (Fed. Cir. 1988).

12. The claims are drawn quite broadly to an isolated polypeptide (1) comprising a fragment of SEQ ID NO:1, wherein the fragment is selected from the group consisting of: M1-P27, M1-V21, M1-A25, M1-F26, I57-R161, L16-P27, E87-Q131, Q131-R161, $80-R147, Q56-T71, C72-

M95, C101-L126, I145-R161, Q56-C72, C78-G100, C101-T122, L144-R161, I57-I115, M1-K55, M1-T117, E108-M163, N107-M163, K110-R161, A28-M163, L22-M163, F26-M163, P27-M163 and combinations thereof; (2) an isolated polypeptide variant of SEQ ID NO:1, wherein one or more amino acid differences between SEQ ID NO: 1 and the variant are selected from the group consisting of amino acid positions 1-27, 50, 80, 148, 156, 71,116, 73 and 123 of SEQ ID NO: 1; or (3) an isolated polypeptide encoded by a polynucleotide comprising a portion of the polynucleotide sequence of SEQ ID NO:2 that uniquely identifies SEQ ID NO:2. While the Specification discloses a protein comprising the amino acid sequence SEQ ID NO:1 which is encoded by a polynucleotide that is differentially expressed in lung tumor tissue and fibroblasts isolated from patients with Tangier disease as compared to normal controls (See pg 94, ¶ [0389]-[0390]), it does not teach a commensurate number of the claimed polypeptides. Other than the polypeptide of SEQ ID NO:1, the disclosure fails to provide sufficient guidance and information regarding the structural and functional requirements commensurate in scope with what is encompassed by the instant claims. The disclosure has not shown (1) how to use a polypeptide that comprises a combination of fragments of SEQ ID NO:1; (2) what modifications e.g., substitutions, deletions, or additions) one can make at positions 50, 80, 148, 156, 71, 116, 73, and 123 of SEQ ID NO:1 that will result in protein mutants or variants with the same function/activity as the protein of SEQ ID NO:1, especially in view of the fact that Table 3 identifies these as potential phosphorylation or glycosylation sites; and (3) any guidance on how to use the variants of SEQ ID NO:1 which would, based on the language of said claims, encompass both active and inactive variants, especially in the absence of any functional limitations in the claims. Moreover, the disclosure has not shown which portions of SEQ ID

NO:2 are unique to SEQ ID NO:2 (See 112(2) rejection below). The state of the art is such that the relationship between the sequence of a protein and its activity is not well understood and unpredictable, and that certain positions in the sequence are critical to the protein's structure/function relationship and can only tolerate only relatively conservative substitutions or no substitutions.

13. The problem of predicting protein and DNA structure from sequence data and in turn utilizing predicted structural determinations to ascertain functional aspects of the protein and DNA is extremely complex. While it is known that many amino acid substitutions are generally possible in any given protein, the positions within the protein's sequence where such amino acid substitutions can be made with a reasonable expectation of success are limited. Certain positions in the sequence are critical to the protein's structure/function relationship, e.g. such as various sites or regions directly involved in binding, activity and in providing the correct three-dimensional spatial orientation of binding and active sites. These regions can tolerate only relatively conservative substitutions or no substitutions (see Wells, 1990, Biochemistry 29:8509-8517; Ngo et al., 1994, The Protein Folding Problem and Tertiary Structure Prediction, pp. 492-495). However, Applicant has provided little or no guidance beyond the mere presentation of sequence data to enable one of ordinary skill in the art to determine, without undue experimentation, the positions in the protein which are tolerant to change (e.g. such as by amino acid substitutions or deletions), and the nature and extent of changes that can be made in these positions and still retain the activity of the protein of SEQ ID NO:1.

14. Although the Specification outlines art-recognized procedures for producing variants, and the claims have been amended to recite certain positions in the amino acid sequence to change,

this is not adequate guidance as to the nature of the variants that may be constructed, but is merely an invitation to the artisan to use the current invention as a starting point for further experimentation. While it is noted that claim 129 has been amended to recite specific positions in the amino acid sequence of SEQ ID NO:1 which are to be changed, there is no guidance as to what modifications e.g., substitutions, deletions, or additions) one can make at positions 50, 80, 148, 156, 71, 116, 73, and 123 of SEQ ID NO:1 that will result in protein mutants or variants with the same function/activity as the protein of SEQ ID NO:1, especially in view of the fact that Table 3 identifies these as potential phosphorylation or glycosylation sites. Furthermore, while it is routine in the art to use fragments of a polypeptide to make antibodies, for example, there is no guidance of how to use a polypeptide that comprises a combination of fragments. Moreover, even if an active or binding site for the polypeptide of SEQ ID NO:1 were identified in the specification, that may not be sufficient, as the ordinary artisan would immediately recognize that an active or binding site must assume the proper three-dimensional configuration to be active, which conformation is dependent upon surrounding residues; therefore substitution of non-essential residues can often destroy activity. The art recognizes that function cannot be predicted from structure alone (Skolnick et al., 2000, Trends in Biotech. 18(1):34-39, especially p. 36 at Box 2; previously cited by Applicant).

15. Due to the large quantity of experimentation necessary to generate the infinite number of derivatives recited in the claims and possibly screen same for activity, the lack of direction/guidance presented in the specification regarding which structural features are required in order to provide activity, the absence of working examples directed to same, the complex nature of the invention, the state of the prior art which establishes the unpredictability of the

effects of mutation on protein structure and function, and the breadth of the claims which fail to recite any structural or functional limitations, undue experimentation would be required of the skilled artisan to make and/or use the claimed invention in its full scope.

Claim Rejections - 35 USC § 112, 1st Paragraph (Written Description)

16. Claims 130 and 132 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

17. Claim 130 is drawn to an isolated polypeptide encoded by a polynucleotide comprising a portion of the polynucleotide sequence of SEQ ID NO:2 that uniquely identifies SEQ ID NO:2. The claims also recite wherein the polypeptide is produced by culturing a cell transformed with a polynucleotide comprising a portion of the polynucleotide sequence of SEQ ID NO:2 that uniquely identifies SEQ ID NO:2 under conditions suitable for expression of the polypeptide, and recovering the polypeptide so expressed.

18. To provide adequate written description and evidence of possession of a claimed genus, the specification must provide sufficient distinguishing identifying characteristics of the genus. The factors to be considered include disclosure of compete or partial structure, physical and/or chemical properties, functional characteristics, structure/function correlation, methods of making the claimed product, or any combination thereof. In this case, without being in possession of every polynucleotide sequence in existence, including those yet to be discovered, it cannot be ascertained what portion of SEQ ID NO:2 would be unique to SEQ ID NO:2 (See 112(2)

rejection below). Therefore, without the identification of a particular portion of SEQ ID NO:2 that would be unique to SEQ ID NO:2, the skilled artisan cannot envision the detailed chemical structure of the encompassed polypeptides. Accordingly, in the absence of sufficient recitation of distinguishing identifying characteristics, the specification does not provide adequate written description of the claimed genus. Additionally, the description of one polypeptide species (SEQ ID NO:1) and one polynucleotide species (SEQ ID NO:2) is not adequate written description of an entire genus of functionally equivalent polypeptides, which incorporate all fragments, variants, and derivatives encompassed by the claims.

19. *Vas-Cath Inc. v. Mahurkar*, 19USPQ2d 1111, clearly states that "applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession *of the invention*. The invention is, for purposes of the 'written description' inquiry, *whatever is now claimed"* (See page 1117). The specification does not "clearly allow persons of ordinary skill in the art to recognize that [he or she] invented what is claimed" (See *Vas-Cath* at page 1116).

20. With the exception of the sequences referred to above, the skilled artisan cannot envision the detailed chemical structure of the encompassed polypeptides, and therefore conception is not achieved until reduction to practice has occurred, regardless of the complexity or simplicity of the method of isolation. Adequate written description requires more than a mere statement that it is part of the invention and reference to a potential method of isolating it. The nucleic acid itself is required. See *Fiers v. Revel*, 25 USPQ2d 1601 at 1606 (CAFC 1993) and *Amgen Inc. v. Chugai Pharmaceutical Co. Ltd.*, 18 USPQ2d 1016.

21. One cannot describe what one has not conceived. See *Fiddes v. Baird*, 30 USPQ2d 1481 at 1483. In *Fiddes*, claims directed to mammalian FGF's were found to be unpatentable due to lack of written description for that broad class. The specification provided only the bovine sequence.

22. Therefore, only an isolated polypeptide encoded by a polynucleotide comprising the nucleic acid sequence SEQ ID NO:2, but not the full breadth of the claim meets the written description provision of 35 U.S.C. §112, first paragraph. Applicant is reminded that *Vas-Cath* makes clear that the written description provision of 35 U.S.C. §112 is severable from its enablement provision (see page 1115).

Claim Rejections - 35 USC § 112, 2nd Paragraph

23. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

24. Claims 130 and 132 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

25. Claim 130 is rejected as being indefinite for reciting the phrase "uniquely identifies". Since the claim is drawn to an isolated polypeptide encoded by a polynucleotide comprising a portion of SEQ ID NO:2 that "uniquely identifies SEQ ID NO:2", it is unclear what the term "uniquely identifies" encompasses. Without being in possession of every polynucleotide sequence in existence, including those yet to be discovered, the metes and bounds of the claim

cannot be determined since it cannot be ascertained what portion of SEQ ID NO:2 would be unique to SEQ ID NO:2.

26. Claim 132 is rejected for depending from an indefinite claim.

Claim Rejections - 35 USC § 102

27. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

28. Claim 128 is rejected under 35 U.S.C. 102(b) as being anticipated by Clark et al. (WO 88/00206, published 14 January 1988; cited in the previous Office action). The basis for this rejection is set forth for claims 126-131 at pg 11-12 of the previous Office action (mailed 14 May 2008).

29. Clark et al. teach an isolated IL-6 polypeptide set forth in Fig. 1 that *comprises* the following fragments of SEQ ID NO:1 that are set forth in the claim: M1-P27, M1-V21, M1-A25, M1-F26, L16-P27, Q131-R161, Q56-T71, I145-R161, and K110-R161 (See sequence alignment provided in the previous Office action). It is noted that the term "comprising" in the claim is open language, and thus the claim is not limited to fragments of SEQ ID NO:1 consisting of the recited amino acid residues, but may include additional amino acids flanking either end of the fragment. Thus, the Clark et al. reference meets all the limitations of claim 128.

Summary

30. Claims 128-130 and 132 stand rejected, claim 131 is objected to, and claims 126-127 are allowable.

31. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Advisory Information

Any inquiry concerning this communication or earlier communications from the examiner should be directed to **Jon M. Lockard** whose telephone number is **(571) 272-2717**. The examiner can normally be reached on Monday through Friday, 7:00 AM to 4:30 PM. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, **Manjunath N. Rao**, can be reached on **(571) 272-0939**.

The fax number for the organization where this application or proceeding is assigned is **571-273-8300**.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at **866-217-9197** (toll-free).

/J. M. L./
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November 17, 2008

/Christine J Saoud/
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